

REMARKS

Amendments to the Specification

The specification has been amended to incorporate the substitute sequence listing into the specification and to update the sequence listing paragraph.

No new matter has been added by way of these amendments.

Amendments to the Claims

With the present submission, claims 1, 3, 13-21, and 30-31 have been amended. Claims 2, 4-12, 22-29, and 32-35 have been canceled without prejudice or disclaimer. New claims 36-47 have been added. As such, claims 1, 3, 13-21, 30-31, and 36-47 are under consideration.

Claim 1 has been amended to recite "[a] chemically modified nucleic acid molecule, wherein: a) said nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides; b) each strand of said nucleic acid molecule is independently 18 to 27 nucleotides in length; c) an 18 to 27 nucleotide sequence of the antisense strand of the nucleic acid molecule is complementary to a human NOGO receptor RNA sequence comprising SEQ ID NO: 325; d) an 18 to 27 nucleotide sequence of the sense strand of the nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human NOGO receptor RNA sequence; e) about 50 to 100 percent of the nucleotides in the sense strand and about 50 to 100 percent of the nucleotides in the antisense strand are chemically modified with modifications independently selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications; and f) one or more of the purine nucleotides in one or both strands of the nucleic acid molecule are 2'-O-methyl purine nucleotides and one or more of the pyrimidine nucleotides present in one or both strands of the nucleic acid molecule are 2'-deoxy-2'-fluoro pyrimidine nucleotides." Support for amended claim 1 can be found in the as-filed application at, for example, page 10, line 4, to page 11, line 5; page 14, line 3, to page 16, line 17; page 19, lines 10-30; page 21, lines 12-22; page 23, lines 17-18; page 25, lines 1-23; page 27, line 30, to page 28, line 20; page 37, lines 8-25; page 42, lines 3-22; page 46, line 18, to page 49, line 20; page 80, lines 1-12; page 83, lines 4-8; Figure 16; Tables (I), (II), and (III); and elsewhere.

Claims 13-16, 18-21, and 30 have been amended to depend from claim 1. The term "siNA" has been replaced with the term "nucleic acid" in each of claims 3, 13-21, and 30-31, to insure proper

antecedent basis. These particular amendments do not change the scope of the affected claims. The terms "sense region" and "antisense region" have been replaced with the terms "sense strand" and "antisense strand," respectively, in claims 13-16, 18-21, and 30, also to insure proper antecedent basis. Furthermore, the term "1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the" have been inserted before each of the terms "pyrimidine nucleotides" and/or "purine nucleotides" in claims 13-15, and 18-20, to more particularly point out the number of the recited nucleotides present in the specified strands. The term "terminal" has been inserted before the term "phosphorothioate internucleotide linkage" in claim 21, and before the term "phosphate group" in claim 30, to more particularly point out the terminal location of these groups on the designated strands. Other amendments to these claims have been made to correct unintended typographic errors, and/or to improve grammatical coherence. Support for these amendments can be found in various places in the as-filed application. For example, support for amended claim 13 can be found in the as-filed application at, *inter alia*, page 21, lines 10-12. Support for amended claim 14 can be found in the as-filed application at, *inter alia*, page 21, lines 10-12. Support for amended claim 15 can be found in the as-filed application at, *inter alia*, page 21, lines 15-17. Support for amended claim 16 can be found in the as-filed application at, *inter alia*, page 37, line 8, to page 38, line 30. Support for amended claim 17 can be found in the as-filed application at, *inter alia*, page 28, lines 20-23; page 43, line 20, to page 44, line 10; page 50, lines 27-30. Support for amended claim 18 can be found in the as-filed application at, *inter alia*, page 21, lines 17-20. Support for amended claim 19 can be found in the as-filed application at, *inter alia*, page 21, lines 17-20; page 23, lines 17-18. Support for amended claim 20 can be found in the as-filed application at, *inter alia*, page 23, lines 10-17. Support for as-amended claim 21 can be found in the as-filed application at, *inter alia*, page 31, lines 6-8; page 36, line 15, to page 37, line 7. Support for amended claim 30 can be found in the as-filed application at, *inter alia*, page 35, line 21, to page 36, line 14. Support for amended claim 31 can be found in the as-filed application at, *inter alia*, page 30, lines 20-21.

New claim 36 depends from claim 1, reciting "[t]he nucleic acid molecule of claim 1, wherein 1, 2, or 3 of the purine nucleotides present in the sense strand are 2'-O-methyl purine nucleotides." Support for new claim 36 can be found in the as-filed application at, for example, page 21, lines 12-15; page 28, lines 11-13; and elsewhere.

New claim 37 also depends from claim 1, reciting "[t]he nucleic acid molecule of claim 1, wherein the antisense strand, sense strand, or both ... include a 3'-overhang of 1-3 nucleotides." Support for new claim 37 can be found in the as-filed application at, for example, page 15, lines 24-28; page 31, lines 6-17; and elsewhere.

New claim 38 depends from claim 37, reciting the molecule of claim 37 wherein the nucleotides of the 3'-overhang are chemically modified as specified. Support for new claim 38 can be found in the as-filed application at, for example, page 21, lines 20-21; page 31, lines 6-17; and elsewhere.

New claim 39 depends from claim 1, reciting the molecule of claim 1, further including "1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more phosphorothioate internucleotide linkages" in one or both strands. Support for new claim 39 can be found in the as-filed application at, for example, page 31, line 29, to page 33, line 3; page 36, line 15, to page 37, line 7.

New claim 40 also depends from claim 1, reciting the molecule of claim 1, further including "1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more 2'-methoxyethyl (MOE) nucleotides" in one or both strands. Support for new claim 40 can be found in the as-filed application at, for example, page 54, line 27, to page 55, line 11, and elsewhere.

New claim 41 depends from claim 1, reciting the molecule of claim 1, further including "1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more locked nucleic acid (LNA) nucleotides" in one or both strands. Support for new claim 41 can be found in the as-filed application at, for example, page 50, lines 1-26, and elsewhere.

New claim 42 is independent, reciting "[a] chemically modified nucleic acid molecule comprising a sense strand and a separate antisense strand, wherein: a) each strand of said nucleic acid molecule is independently 18 to 27 nucleotides in length; b) an 18 to 27 nucleotide sequence of the antisense strand of said nucleic acid molecule is complementary to a human NOGO receptor RNA sequence comprising SEQ ID NO: 325; c) an 18 to 27 nucleotide sequence of the sense strand of said nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human NOGO receptor RNA sequence; d) the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends; e) one or more of the nucleotides present in the sense strand and one or more of the nucleotides present in the antisense strand are 2'-O-methyl modified nucleotides; and f) one to ten or more of the pyrimidine nucleotides present in the sense strand and one to ten or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides." Support for new claim 42 can be found in the as-filed application at, for example, page 10, line 4, to page 11, line 5; page 14, line 3, to page 16, line 17; page 19, lines 10-30; page 21, lines 12-22; page 23, lines 17-18; page 25, lines 1-23; page 27, line 30,

to page 28, line 20; page 37, line 8, to page 38, line 30; page 42, lines 3-22; page 46, line 18, to page 49, line 20; page 80, lines 1-12; page 83, lines 4-8; Figure 16; Tables (I), (II), and (III); and elsewhere.

New claim 43 depends from claim 42, reciting "[a] composition comprising the nucleic acid molecule of claim 42 in a pharmaceutically acceptable carrier or diluent." New claim 43 finds support in the as-filed application at, for example, page 30, lines 20-21, and elsewhere.

New claim 44 is independent, reciting "[a] chemically modified nucleic acid molecule, wherein: a) the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides; b) each strand of the nucleic acid molecule is independently 18 to 27 nucleotides in length; c) an 18 to 27 nucleotide sequence of the antisense strand of the nucleic acid molecule is complementary to a human NOGO receptor RNA sequence comprising SEQ ID NO: 325; d) an 18 to 27 nucleotide sequence of the sense strand of the nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human NOGO receptor RNA sequence; e) at least 50 percent of the nucleotides of each strand of said nucleic acid molecule are modified nucleotides having a sugar modification selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, and deoxyabasic modifications; f) at least one of said sugar modifications is a 2'-O-methyl modifications; and g) each strand of said nucleic acid molecule has no more than 3 consecutive ribonucleotides." New claim 44 finds support in the as-filed application at, for example, page 10, line 4, to page 11, line 5; page 14, line 3, to page 16, line 17; page 19, lines 10-30; page 21, lines 12-22; page 23, lines 17-18; page 25, lines 1-23; page 27, lines 4-30; page 28, line 28, to page 30, line 19; page 37, lines 8-25; page 42, lines 3-22; page 46, line 18, to page 49, line 20; page 80, lines 1-12; page 83, lines 4-8; Figure 16; Tables (I), (II), (III); and (IV); and elsewhere.

New claim 45 depends from claim 44, reciting a composition comprising the molecule of claim 44 "in a pharmaceutically acceptable carrier or diluent." New claim 45 finds support in the as-filed application at, for example, page 30, lines 20-21.

New claim 46 recites "[a] method of modulating the expression of human NOGO receptor gene in a cell, comprising administering the chemically modified nucleic acid molecule of claim 1 to the cell under conditions suitable for modulating the expression of NOGO receptor gene in the cell." New claim 46 finds support in the as-filed application at, for example, page 56, line 4, to page 57, line 6; page 59, lines 10-23; and elsewhere.

New claim 47 recites "[a] method of modulating the expression of human NOGO receptor gene in a cell, comprising administering the chemically modified nucleic acid molecule of claim 44 to the cell under conditions suitable for modulating the expression of NOGO receptor gene in the cell." New claim 47 finds support in the as-filed application at, for example, page 56, line 4, to page 57, line 6; page 59, lines 10-23; and elsewhere.

Amendments to and cancellations of claims are made without prejudice or disclaimer, and do not constitute amendments to overcome any prior art or other statutory rejections. They are fully supported by the specification as filed, as explained above, and thus do not introduce new matter. Additionally, these amendments and cancellations are not and should not be construed as admissions regarding the patentability of the claimed or canceled subject matter. Applicants reserve the right to pursue the subject matter of previously presented claims in this or in any other appropriate patent application. Accordingly, Applicants respectfully request the entry of the amendments presented herein.

The Sequence Listing

Applicants have enclosed a substitute sequence listing and request its entry in place of the previously entered sequence listing. The substitute sequence listing adds SEQ ID NO: 325. SEQ ID NO: 325 represents GenBank Accession No. NM_023004.2, which was disclosed in the as-filed application at, for example, page 165 and original claim 32. The version of NM_023004.2 appearing in the herein submitted sequence listing as SEQ ID NO: 325 appeared in GenBank on March 3, 2001, which is also included in the U.S. Provisional patent application No. 60/363,124 priority application (*see* page 287). Accordingly the substitute sequence listing adds no new matter and Applicants respectfully request its entry.

The Restriction Requirement

The Office alleged that claim 33 is subject to restriction under 35 U.S.C. § 121. *See* Restriction Requirement, at page 2. Specifically, the Office alleged that claim 33 "is not considered to be a proper genus/Markush." *Id.* The Office required that Applicants "elect one (1) siNA sequence (*i.e.*, SEQ ID NO.) from claim 33. *Id.* at page 3.

With the present submission, claim 33 has been canceled. It is Applicants' good faith belief that the outstanding Restriction Requirement is moot and an election on its basis is no longer necessary.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully urge early action on the merits. If the Examiner believes a teleconference will advance prosecution, she is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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